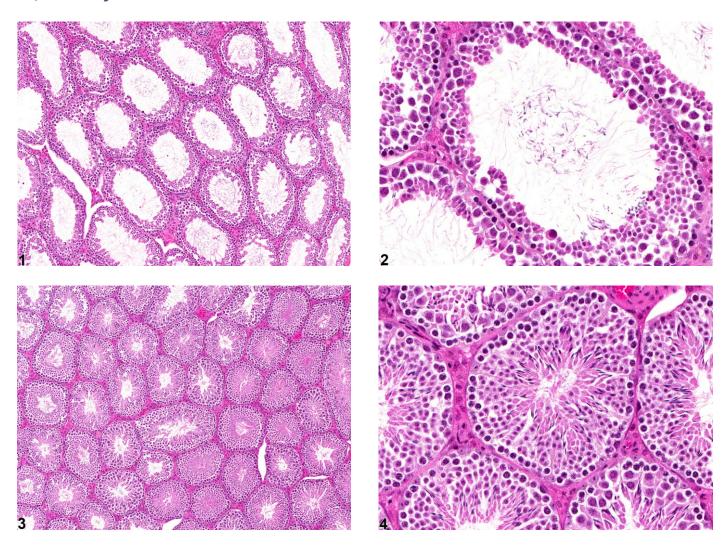


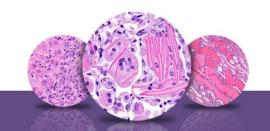


### Testis, Seminiferous tubule - Dilation



**Figure Legend: Figure 1** Testis, Seminiferous tubule - Dilation in a male B6C3F1 mouse from a chronic study. These seminiferous tubules are dilated. **Figure 2** Testis, Seminiferous tubule - Dilation in a male B6C3F1 mouse in a chronic study. This higher magnification of Figure 1 shows a dilated seminiferous tubule with a reduced population of germinal epithelium. **Figure 3** Testis - Normal in a male B6C3F1 mouse from a chronic study. Normal seminiferous tubules for comparison with Figure 1. **Figure 4** Testis - Normal in a male B6C3F1 mouse from a chronic study. Normal seminiferous tubules for comparison with Figure 2.





### Testis, Seminiferous tubule - Dilation

Comment: Seminiferous tubule dilation is characterized by increased luminal diameter of the seminiferous tubules (Figure 1 and Figure 2). This contrasts with the inconspicuous luminal space in the seminiferous tubules from a normal testis (Figure 3 and Figure 4). The affected tubules have thinning and compression of the seminiferous epithelium, which is caused by pressure buildup from increased volume of seminiferous tubule fluid within the lumen. The increased fluid can be due to decreased reabsorption of fluid in the efferent ducts, efferent duct blockage, decreased emptying of fluid from the seminiferous tubules, or increased production of seminiferous tubule fluid by the Sertoli cells. If the fluid pressure is maintained, the tubular dilation can rapidly progress to severe germinal epithelial atrophy, resulting in an irreversible cessation of spermatogenesis. When the tubular dilation is secondary to blockage of the efferent ducts, the lesion may be unilateral, and yet the cause of the blockage can still be test article related. Unless the efferent ducts are sampled (which is difficult in rodents), the cause of the tubular dilation will not be apparent. The ERKO mouse develops seminiferous tubular dilation followed by severe germinal epithelial atrophy as it reaches puberty. This occurs as a secondary consequence to the failure of the efferent ducts to resorb seminiferous tubule fluid, which is an estrogen-dependent function. Seminiferous tubular dilatation with its sequel of atrophy has been reported for a number of chemicals, including the fungicide carbendazim, a PDE4 inhibitor, a leukotriene inhibitor, and endothelin antagonists.

**Recommendation:** Tubular dilatation should be diagnosed and graded and should be discussed in the pathology narrative if the incidence and/or severity appears to be related to chemical administration. When present, bilateral involvement should be recorded because unilaterality usually reflects a secondary response to lesions in the efferent ducts. Attention should also be paid to the incidence of unilateral or bilateral seminiferous tubule atrophy since this can be a progressive and end-stage lesion of tubular dilation. Attention should also be paid to any evidence of gross or microscopic lesions within the initial segment of the epididymis or the epididymal fat pad (location of the efferent ducts) that may reflect sperm granulomas, sperm stasis, or dilated ducts, which would indicate the likely origin of the initiating, obstructive lesion.



### Testis, Seminiferous tubule - Dilation

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